MEDICATION UPDATES

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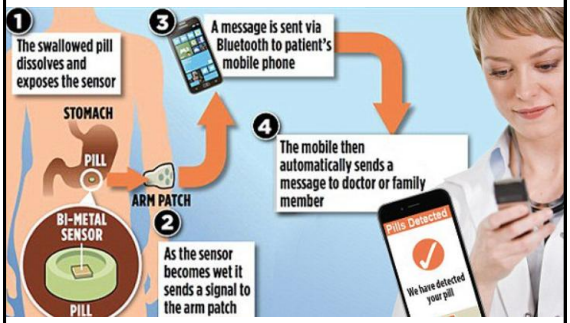
Pharmacy Alternatives

Antipsychotics

Abilify MyCite®

- FDA approved on November 13, 2017
- First drug in the US with a digital ingestion tracking system
- When ingested, a sensor in the pill sends a message to a wearable patch
- The patch transmits information to a mobile application
- This allows the user to track the ingestion (adherence) of the medication
- Patients may opt to share this information with caregivers/physicians through a web-based portal



http://thasso.com/abilify-mycite-the-first-digital-pill-where-does-all-that-silicon-go/

Vraylar® (Cariprazine)

- Atypical antipsychotic approved by the FDA on September 17, 2015
- Once-daily oral dosing
- Schizophrenia: 1.5mg – 6mg / day
- Bipolar disorder: 3mg – 6mg / day
- BBW: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.
  - Cariprazine is NOT approved for the treatment of patients with dementia-related psychosis

Vraylar® (Cariprazine)

- Mechanism of Action and pharmacodynamics
  - Partial agonism and antagonism
- Receptor activity
  - D2 activity
  - 5-HT1a activity
  - 5-HT 2a activity
  - D3 activity

Vraylar® (Cariprazine) Common Side Effects

- Indigestion (4% - 7%)
- Vomiting (4% - 10%)
- Akathisia
  - Schizophrenia: 9%
  - Bipolar: 20%
- EPS
  - Schizophrenia: 15%
  - Bipolar: 26%
- Somnolence (5% - 8%)
- Restlessness (4% - 7%)

Vraylar® (Cariprazine) Pearls

- Available as 1.5mg, 3mg, 4.5mg, and 6mg oral capsules
- May be taken with or without food
- Avoid dehydration or overheating (potential for disruption in body temperature regulation)
- For diabetic patients, monitor for symptoms of hyperglycemia and report difficulties with glycemic control
- Report symptoms of hypotension with initial dosing and dose changes
- Report symptoms of neuroleptic malignant syndrome or tardive dyskinesia

Rexulti® (Brexpiprazole)

- Atypical antipsychotic approved by FDA on July 10, 2015 for treatment of schizophrenia and as an adjunct to antidepressants for major depressive disorder
- Developed by Otsuka (creators of Abilify)
- Once-daily oral dosing
- Schizophrenia: 1mg – 4mg / day
- Major depressive disorder (adjunct): 0.5mg – 3mg / day
- BBW:
  - Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death
    - Brexpiprazole is not approved for the treatment of patients with dementia-related psychosis
  - Increased risk of suicidal thinking and behavior was found in children, adolescents, and young adults taking antidepressants
    - Monitor for worsening and emergence of suicidal thoughts and behaviors

Rexulti® (Brexpiprazole) Common Side Effects

- Hyperglycemia (9% - 10%)
- Serum triglycerides raised
  - Short-term use: 5% - 13%
  - Long-term use: 13% - 17%
- Weight increased
  - Short-term use: 2% - 11%
  - Long-term use: 20% - 30%
- Akathisia (4% - 14%)
- Extrapyramidal movements excluding akathisia (5% - 6%)
- Headache (4% - 9%)
- Compared to aripiprazole, may have a decreased risk for agitation and restlessness

Rexulti® (Brexpiprazole) Pearls

- Available as 0.25mg, 0.5mg, 1mg, 2mg, 3mg, and 4mg oral tablets
- May be taken with or without food
- Avoid dehydration or overheating (potential for disruption in body temperature regulation)
- Report worsening depression, suicidal ideation, or unusual changes in behavior
- Report symptoms of orthostatic hypotension, tardive dyskinesia, or neuroleptic malignant syndrome.

Invega® (Paliperidone Palmitate)

- Atypical antipsychotic commonly used for the treatment of mania, bipolar disorder, schizoaffective disorder, and schizophrenia
- BBW: Risk of death is increased in elderly patients with dementia-related psychosis treated with antipsychotic drugs
  - Paliperidone palmitate is NOT approved for use in patients with dementia-related psychosis
- In addition to oral formulation, newer injectable formulations are available
- Invega Sustenna: once monthly injection
- Invega Trinza: quarterly (once every 3 months) injection
  - Can be started after 4 consecutive Invega Sustenna injections, with the last 2 being the same strength

Invega® (Paliperidone Palmitate) Side Effects

- Injection site reaction (up to 12%)
- Hyperprolactinemia (32% - 55.6%)
- Weight gain (5.8% to 18.4%)
- Akathisia (1% - 11%)
- Dizziness (1% - 6%)
- EPS (up to 12%)
- Headache (6% - 15%)
- Parkinsonism (4% - 18%)
- Agitation (4% - 10%)

Invega® (Paliperidone Palmitate) Serious Side Effects (<1%)

- Orthostatic hypotension
- Prolonged QT interval
- Syncope
- Agranulocytosis/Leukopenia/Neutropenia
- Anaphylaxis
- Seizure
- Tardive dyskinesia
- Tonic-clonic seizure
- Priapism
- Neuroleptic malignant syndrome

Diabetes Medications

Invokana® (Canagliflozin) BBW

- Updated BBW:
- In patients with T2DM who have established CVD or at risk for CVD, canagliflozin has been associated with lower limb amputations, most frequently of the toe and midfoot; some also involved the leg
- Before initiating, consider factors that may increase amputation risk.
  - Monitor for infections or ulcers of lower limbs. Discontinue if these occur.

Insulins

- Basaglar®
- Tresiba®
- Ryzodeg® 70/30

Basaglar® (Insulin Glargine)

- Long-acting basal insulin
  - Microcrystals slowly release insulin over 18 – 26 hours
  - Tmax = 12 hours
- 100 U/mL
  - Toujeo®: 300 U/mL
- Side effects include injection site reactions, lipodystrophy, pruritus, rash, edema, or weight gain
- Never mix/dilute with any other insulin or solution
- Administer at same time each day

Tresiba® (Insulin Degludec)

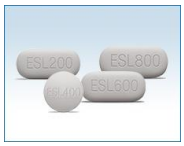
- Ultra-long-acting basal insulin
  - Lasts up to 42 hours
  - Tmax = 9 hours
- 100 U/mL and 200 U/mL
- Side effects include injection site reactions, pruritus, rash, edema, lipodystrophy, and weight gain
- Limit alcohol use with drug
- Inject a missed dose during waking hours and ensure at least 8 hours have elapsed between consecutive injections

Ryzodeg® 70/30 (Insulin Degludec/Aspart)

- Insulin Degludec: long acting
- Insulin Aspart: rapid acting
  - Tmax = 72 minutes
- 100 U/mL
- Once or twice daily with meals
- Side effects include nasopharyngitis, upper respiratory tract infection, influenza, allergic reaction, injection site reaction, peripheral edema, weight gain, or headache
- May cause hypoglycemia, which impairs ability to concentrate → avoid activities requiring alertness/coordination until effects are fully realized
- If a dose is missed, take with next main meal of day

Anticonvulsants

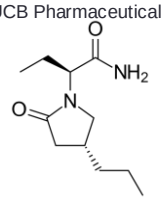
Briviact® (Brivaracetam)



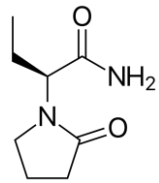
Aptiom® (Eslicarbazepine Acetate)

Briviact® (Brivaracetam)

- Anticonvulsant approved for the treatment of partial seizures by the FDA on February 18, 2016
- Chemical analog of levetiracetam (also developed by UCB Pharmaceuticals)



Briviact® (Brivaracetam)



Keppra® (Levetiracetam)

Briviact® (Brivaracetam)

- Twice-daily dosing
- IV solution: 10mg/mL
- Oral solution: 10mg/mL
  - May be given via gastrostomy or nasogastric tube
  - Dilution is not necessary
  - Use within 5 months of opening
- Oral tablet: 10mg, 25mg, 50mg, 75mg, 100mg
  - May give with our without food
  - Swallow whole with liquid (do not crush or chew)

Briviact® (Brivaracetam) Common Side Effects

- Nausea/Vomiting (5%)
- Dizziness (12%)
- Fatigue (9%)
- Constipation
- Irritability

Briviact® (Brivaracetam) Pearls

- Avoid activities requiring mental alertness/coordination until full effects are realized
- Report worsening depression, suicidal ideation, or unusual changes in behavior
- Report psychiatric symptoms, such as anxiety, aggression, agitation, psychosis, hallucinations, or paranoia
- Do not discontinue abruptly due to potential for increased seizures or status epilepticus

Aptiom® (Eslicarbazepine Acetate)

- Anticonvulsant approved by the FDA on August 28, 2015 for monotherapy treatment of partial seizures
  - Previously approved as adjunct therapy to partial seizures
  - Potential use for treatment of trigeminal neuralgia
- Prodrug → inactive form gets metabolized to the active metabolite eslizcarbazepine
  - Similar to how oxcarbazepine (inactive) gets metabolized to its active form lizcarbazepine
  - Eslizcarbazepine is an isomer of lizcarbazepine
- Once-daily dosing
- Oral tablet: 200mg, 400mg, 600mg, 800mg (all but 400mg scored)

Aptiom® (Eslicarbazepine Acetate) Common Side Effects

- Nausea (10% - 16%)
- Vomiting (6% - 10%)
- Ataxia (4% - 6%)
- Dizziness (19% - 28%)
- Headache (13% - 15%)
- Somnolence (11% - 18%)
- Tremor (2% - 4%)
- Vertigo (2% - 6%)
- Blurred vision (5% - 6%)
- Diplopia (9% - 11%)
- Fatigue (4% - 7%)

Aptiom® (Eslicarbazepine Acetate) Serious Side Effects

- Stevens-Johnson syndrome
- Toxic epidermal necrolysis
- Hyponatremia (2%)
- Increased liver enzymes
- Visual impairment (1% - 2%)
- Suicidal thoughts

Aptiom® (Eslicarbazepine Acetate) Administration

- May be crushed
- May give with or without food
- National Institute for Occupational Safety and Health (NIOSH) recommends use of single gloves by anyone handling intact tablets or capsules or administering from a unit-dose package
- For preparations including cutting, crushing, manipulating, or handling of uncoated tablets, use double gloves and a protective gown. If possible, use a ventilated control device or respiratory protection. Wear single gloves and eye/face protection if formulation is hard to swallow or if patient may resist, vomit, or spit.

Aptiom® (Eslicarbazepine Acetate) Administration

- Not a controlled substance
- No drug interactions with many other anti-seizure medications with exception of inducing products: phenytoin, phenobarbital and carbamazepine
- Should not be used with oxcarbazepine
- Once weekly stepwise titration to 800-1600mg
- May be used as adjunctive and monotherapy
- No autoinduction
- No laboratory monitoring or levels required

On the Horizon…

Treatment of ADHD in Women of Reproductive Age

- Exposure of fetus to *methylphenidate* was associated with an increased risk of cardiac malformations
- Exposure of fetus to *amphetamines* was not associated with an increased risk of cardiac malformations
- In the future, prescribers may be more inclined to treat women of child-bearing age with amphetamines rather than methylphenidate

Ketamine

- Promising hope for rapid treatment of suicidal ideation
- Improvement began within one day and persisted for up to seven days
- Ketamine remains investigational due to efficacy and ethical concerns
- Common adverse effects:
  - Hypertension
  - Tachycardia
- Serious adverse effects:
  - Bradyarrhythmia
  - Cardiac dysrhythmia
  - Hypotension
  - Anaphylaxis
  - Apnea
  - Laryngeal spasm
  - Pulmonary edema
  - Respiratory depression

Options to Treat Resistant Depression

- Open label trial with >1500 patients randomly assigned to three groups over twelve weeks:

1. Augment with aripiprazole
2. Augment with bupropion sustained-release
3. Switch to bupropion

Options to Treat Resistant Depression

- Augment with aripiprazole: 29%
  - May be more efficacious in females than males (if true, this success rate may be underestimated)
  - Akathisia, somnolence, and weight gain occurred more often than the bupropion groups
- Augment with bupropion sustained-release: 27%
  - Anxiety was more often reported
- Switch to bupropion: 22%
  - Anxiety was more often reported

Epidiolex®

- Investigational medication based on cannabidiol
- Seeking indication for treatment of seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome
  - Both of these childhood-onset epilepsy disorders are rare and difficult to treat
- Over a 14 week period, 44% saw a significant reduction in drop seizures
- About 1,500 patients are already taking the medications under the FDA's "compassionate use" exception

References

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